DEPARTMENT OF HEALTH & HUMAN SERVICES

9 1793d Food and Drug Administration

Dallas District Office
4040 North Central Expressway
Suite 300
Dallas, Texas 75204

September 27, 2001

Ref: 2001-DAL-WL-38

WARNING LETTER

CERTIFIED MAIL
RETURNED RECEIPT REQUESTED

Mr. Ronald E. Dykes, President
International Science & Technology, L.P.
dba Diamatrix Ltd., Inc.
2203 Timberloch Place, Suite 130
The Woodlands, Texas 77380

Dear Mr. Dykes:

During an inspection of your firm located in the Woodlands, Texas on August 14, 16, and 17, 2001, our investigator determined that your firm manufactures and repacks non-sterile and sterile ophthalmic knives. These products are medical devices as defined in Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

Your devices are adulterated within the meaning of Section 501(h) of the Act in that the methods used in, or the facilities or controls used for their manufacturing, packing, storage, or installation are not in conformance with the Current Good Manufacturing Practice (CGMP) requirements of the Quality System Regulations, as specified in Title 21, Code of Federal Regulation (CFR), Part 820. Significant GMP deviations include, but are not limited to, the following:

1. Failure of management with executive responsibility to ensure that an adequate and effective quality system has been established and maintained [21 CFR 820.20]. For example, your firm has not developed written procedures for a quality policy, quality plan, management review, and quality audit [FDA-483 Item 4].

2. Failure to establish and maintain procedures for implementing corrective and preventive action [21 CFR 820.100]. For example, your firm has not developed written procedures describing how quality data sources are identified and evaluated for corrective and preventive actions [FDA-483 Item 8].

3. Failure to establish and maintain complaint handling procedures [21 CFR 820.198] and MDR procedures [21 CFR 803.17], [FDA-483 Items 1 and 7].

4. Failure to establish and maintain requirements, including quality requirements, that must be met by suppliers and contractors [21 CFR 820.50]. For example, your firm:

   (a) has not developed procedures describing how suppliers are evaluated for quality acceptance requirements [FDA-483 Item 2(a)] and,

   (b) has not developed contract agreements with suppliers and contractors regarding notification of changes in components, products, and services [FDA-483 Item 2(c)].

5. Failure to establish and maintain procedures to control all documents [21 CFR 820.40]. For example, there are no procedures designating an individual(s) to review documents for adequacy and approve them prior to their use [FDA-483 Item 5].

We have received your response letter with attachments, dated September 4, 2001, and received by our office on September 17, 2001, responding to our list of inspectional observations (FDA-483) issued to you at the completion of the inspection. You promised GMP corrections in stages between August 30 and November 30, 2001. Based on the documents submitted thus far, your response is incomplete in fully addressing the underlying issues that may have contributed to the GMP deficiencies. Our reasons are indicated as follows:

FDA-483 Items 1 and 7 (Complaint handling and MDR procedures):

Your response is inadequate. You have not provided training records showing employees are adequately trained on the procedures.

The complaint form does not contain data fields for documenting root cause analyses for device failures, corrective actions taken and results of corrective actions, and essential investigation requirements as required by 21 CFR 820.198(e) (e.g., whether the device was being used for treatment or diagnosis; and the relationship of the device to the reported medical device reporting incident).

The complaint handling procedure and form refer to the medical device reporting procedure (SOP 1002) which is inadequate. For example, the medical device reporting procedure does not (a) establish and describe how each complaint is evaluated against MDR reporting criteria for reporting under the MDR regulation; and (b) specify record keeping requirements as required by 21 CFR 803.18 (MDR Event Files).

FDA-483 Item 2 (Purchasing Controls):

Your response is incomplete. Procedures have not been submitted for our review.

FDA-483 Item 4 (Management Control):

Your response is inadequate. You promised to implement QA audit procedures by October 31, 2001. However, you have not fully addressed other requirements of 21 CFR 820.20, as cited by the observation (i.e., quality policy, quality plan, resources, management representative, and management review).

FDA-483 Item 5 (Document Controls):

Your response is incomplete. Procedures have not been submitted for our review.

FDA-483 Item 8 (CAPA):

Your response is inadequate. Your CAPA Protocol (SOP 10003) does not fully incorporate all requirements of 21 CFR 820.100 (a)(1) through (a)(7) and (b). In SOP 10003, you indicate that if a product is found to have a nonconformance rate of over [redacted] for a specific complaint code over the past [redacted], product will be investigated for root cause of non-conformance. Other than complaint records, you have not identified other quality sources for trend analysis.

You have also not provided past non-conformance data or a rationale to show if [redacted] is an acceptable non-conformance rate of product complaints. In our view, your action for not conducting a root cause analysis when the non-conformance rate is equal to or less than [redacted] may not provide adequate detection of quality problems in relation to health risk analysis for each type of product complaint.

Your devices are also misbranded within the meaning of Section 502(t)(2) of the Act in that a report of correction or removal was not submitted to FDA as required by Section 519(f)(1) of the Act. The Correction and Removal Regulation (21 CFR 806), promulgated under Section 519(f)(1), requires manufacturers and importers to promptly report to FDA, within 10 working days, any correction or removal of a device to reduce a risk to health.

Our inspection revealed that on or about June 14, 2000, your firm notified a number of physicians for product retrieval because you were immediately concerned with the sterility of the ophthalmic knives. Your subsequent investigation with the contract manufacturer revealed that [redacted] sterilization produces a reaction between the cap and the neck of the blade which creates a deposit of contamination on the blade (discoloration which looks like rust). Your firm's action to retrieve the product, based on your initial health assessment, meets the definition of a "removal" as defined in 21 CFR 806.2(i) and 21 CFR 806.10(a)(1), which requires manufacturers and importers to promptly report to FDA any correction or removal of a device if the correction or removal was initiated to reduce a risk to health. You did not report the product removal until the issue was raised by our investigator.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the FDA-483 issued at the close of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems.

You are responsible for investigating and determining the causes of the violations identified by the FDA. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions.

Until these violations are corrected, and FDA has documentation to establish that such corrections have been made, federal agencies will be advised of the issuance of this Warning Letter so that they may take this information into account when considering the award of contracts.

You should take prompt action to correct these violations. Failure to promptly correct these violations may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil penalties.

Please provide this office in writing within 15 working days of receipt of this letter a report of the specific steps you have taken or will take to identify and correct any underlying systems problems necessary to assure that similar violations will not recur. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time frame within which the corrections will be completed. Your reply should be directed to Thao Ta, Compliance Office, at the above letterhead address.

Sincerely,

Michael A. Chappell
Dallas Districe Director

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